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WDN/TMH/DAG:lam 10/12/04 317573
PATENT

Attorney Reference Number 6395-61666-01
Application Number 10/017,168
EXPRESS MAIL LABEL NO. EV331579945US
DATE OF DEPOSIT: OCTOBER 12, 2004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Liu *et al.*
Application No. 10/017,168
Filed: December 14, 2001
Confirmation No. 9437
For: COMPOSITIONS AND METHODS FOR DETECTING TREPONEMA PALLIDUM
Examiner: Vanessa L. Ford
Art Unit: 1645
Attorney Reference No. 6395-61666-01

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TRANSMITTAL LETTER

Enclosed for filing in the application referenced above are the following:

☒ Appeal Brief.
☒ Check no. 111250 in the amount of $340.00 in payment of the appeal fee required by 37 C.F.R. §41.20(b)(2).

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Respectfully submitted,

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APPEAL BRIEF

This Appeal Brief is in furtherance of the Notice of Appeal, mailed on August 30, 2004 with a Certificate of Mailing, and received by the U.S. Patent and Trademark Office on September 2, 2004. In accordance with 37 C.F.R. §41.20(b)(2), a check in the amount of $340 is enclosed in payment of the appeal fee (large entity). If the Commissioner finds that additional fees are required for this filing, deposit account authority is provided on the attached transmittal letter.

Real Party in Interest

The real party in interest is The Government of the United States of America, as represented by the Secretary of the Department of Health and Human Services, Centers for Disease Control and Prevention, who is the assignee of record of the entire interest in the subject application.

Related Appeals and Interferences

To the knowledge of Appellant (who is also Assignee) or Appellant's legal representative, there are no prior or pending appeals, interferences or judicial proceedings that

may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the present appeal.

Status of Claims

Claims 1-29 were filed with the original specification. Thereafter, claims 30-36 were added. Claims 3, 17-26, 29, and 32-36 have been cancelled. Claims 4, 8-10, and 27 have been withdrawn. Claims 1, 2, 5-7, 11-16, 28, 30, and 31 have been considered by the Examiner and are rejected. The present appeal is directed to all of the rejected claims, *i.e.* claims 1, 2, 5-7, 11-16, 28, 30, and 31. A copy of the claims that are being appealed is attached in the Claims Appendix.

Status of Amendments

No amendments have been filed subsequent to the final Office Action, mailed March 2, 2004, which issued final rejections of all of the claims involved in the present appeal (*i.e.*, claims 1, 2, 5-7, 11-16, 28, 30 and 31).

Summary of the Claimed Subject Matter

The appeal involves two independent method claims, *i.e.*, claims 1 and 16.

Claim 1 is directed to a method of detecting *Treponema pallidum* or anti-treponemal antibodies in a biological sample. In this embodiment, an antibody-containing biological sample is contacted with an isolated *T. pallidum* acidic repeat protein or one or more isolated, immunogenic peptide(s) thereof (see, for example, specification at page 17, lines 7-10; page 24, lines 2-5; page 24, line 11 though page 25, line 22). Detection of the formation of a complex between the *T. pallidum* acidic repeat protein or its immunogenic peptide and an antibody in the biological sample indicates the presence of *T. pallidum* or anti-treponemal antibodies in the biological sample. The *T. pallidum* acidic repeat protein or immunogenic peptide(s) recited in claim 1 include the amino acid sequence $EVEDX_1PX_2VVEPASX_3X_4EGGER$, wherein X_1 is A or V; X_2 is K or G; X_3 is E or G; and X_4 is R or H (see, for example, Figures 14-17 and SEQ ID NOs: 20, 22, 24 and 26 of the sequence listing).

Claim 16 is directed to a method of detecting *T. pallidum* in a biological sample. In this embodiment, a biological sample is contacted with an isolated antibody that is specific for an immunogenic peptide of *T. pallidum* acidic repeat protein, wherein such protein includes the amino acid sequence EVEDX$_1$PX$_2$VVEPASX$_3$X$_4$EGGER (wherein X$_1$ is A or V; X$_2$ is K or G; X$_3$ is E or G; and X$_4$ is R or H) (see, for example, Figures 14-17 and SEQ ID NOs: 20, 22, 24 and 26 of the sequence listing). Detection of the formation of a complex between the isolated antibody and an acidic repeat protein or a peptide thereof, if such is in the biological sample, indicates the presence of *T. pallidum* (see, for example, specification at page 7, lines 10-12; page 17, lines 3-7; page 21, lines 20-23; page 25, line 23 through page 27, line 7).

No independent claim involved in the appeal nor any dependent claims argued separately under the provisions of 37 C.F.R. §41.37(c)(1)(vii) includes a means plus function or step plus function limitation within the meaning of 35 U.S.C. §112, sixth paragraph. Accordingly, no structure, material or acts corresponding to each claimed function is described in this summary.

Grounds of Rejection to be Reviewed on Appeal

Appellant requests review of the following grounds of rejection:

1. Claims 16 and 31 have been rejected under 35 U.S.C. §102(b) allegedly as being anticipated by Norgard *et al., J. Clin. Microbiol.,* 20(4):711-717, 1984 (hereafter "Norgard"). This rejection is based solely on the doctrine of inherent anticipation.

2. Claims 1-2, 5-7, 11-16, and 30-31 have been rejected under 35 U.S.C. §102(b) allegedly as being anticipated by Hunter *et al., J. Clin. Microbiol.*, 16(3):483-486, 1982 (hereafter "Hunter"). This rejection is based solely on the doctrine of inherent anticipation.

3. Claim 28 has been rejected under 35 U.S.C. §103(a) allegedly as being obvious in light of Hunter.

Argument

1. Norgard Does Not Inherently Anticipate Claims 16 and 31 under 35 U.S.C. §102(b)

A. The Examiner Made At Least Two Material Factual Errors in This Rejection

As an initial matter, the Examiner has mistaken the subject matter of claims 16 and 31 and has further mistaken the facts of the cited reference, *i.e.*, Norgard. Without a thorough

understanding of the subject matter of claims 16 and 31 or Norgard, the Examiner could not and did not issue a valid rejection supported by proper facts and evidence.

Treponema pallidum is a bacterium that is a causative agent of syphilis (and other diseases). Upon *T. pallidum* infection, one response of a target organism is to produce antibodies against immunogenic components of *T. pallidum*. While *T. pallidum* infection might be observed in a target organism by detecting the stimulus (*e.g.*, *T. pallidum*) or the response (*e.g.*, antibodies specific for *T. pallidum*), methods of detecting the stimulus and methods of detecting the response are distinct and are not interchangeable.

Claims 16 and 31 clearly recite a "method for detecting the presence of ***Treponema pallidum*** in a biological sample." Thus, these claims are clearly directed to detecting the organism (*i.e.*, the stimulus). The Examiner mistakenly indicates that "the claims are direct (sic) to a method of detecting ***T. pallidum* antibodies** in a biological sample" (see, 8/16/04 Advisory Action at page 3; emphasis added). The Examiner similarly mischaracterizes Norgard as "detecting ***anti*-Treponema monoclonal antibodies** in various body fluids" (8/16/04 Advisory Action at pages 2 and 3/2/2004 Office Action at page 4; see also, 8/16/04 Advisory Action at page 3). In fact, Norgard discloses a limited number of monoclonal antibodies "for the detection of . . . **treponemes** present in various body fluids" (see Abstract in Norgard).

Because the Examiner incorrectly concludes that claims 16 and 31 are directed to "a method of detecting ***T. pallidum* antibodies**," she discounts Applicants' arguments filed June 4, 2004 as having "no relevance" because "[t]here is no limitation in the claim as to how many different antibodies can be detected using the claimed method" (see, 8/16/04 Advisory Action at page 3). Moreover, the Examiner finds Applicants' prior responses lacking for "provid[ing] no evidence (side-by-side comparison) that the *T. pallidum* antibodies as detected by Norgard et al differ from the *T. pallidum* antibodies detected in the claimed method" (see, 8/16/04 Advisory Action at page 3). The claim limitation and evidence referred to by the Examiner are irrelevant to the method of detecting ***T. pallidum*** in claims 16 and 31.

This rejection of claims 16 and 31 should be withdrawn at least because the Examiner failed to thoroughly understand the claims and the cited reference prior to issuing the rejection. As a result, the Examiner has not supported her rejection of the **claimed** subject matter, as she must for this rejection to stand. Applicants request that this rejection be overturned.

B. *Irregardless of the Examiner's Factual Errors, Norgard Does Not Inherently Disclose At Least One Limitation of Claims 16 and 31 and, Therefore, Norgard Does Not Anticipate These Claims*

To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently (see, *e.g.*, Glaxo Inc. v. Novopharm Ltd., 52 F.3d 1043, 1047, 34 USPQ2d 1565, 1567 (Fed. Cir. 1995)).

At least one limitation of claims 16 and 31 is not expressly or inherently disclosed by Norgard. In particular, claims 16 and 31 recite, in relevant part, isolated anti-*T. pallidum* antibodies ". . . specific for an immunogenic peptide of *T. pallidum* acidic repeat protein . . . compris[ing] the amino acid sequence $EVEDX_1PX_2VVEPASX_3X_4EGGER$, wherein X_1 is A or V; X_2 is K or G; X_3 is E or G; and X_4 is R or H . . . ." By relying solely on the doctrine of inherent anticipation, the Examiner admits that Norgard does not expressly disclose a method of detecting *T. pallidum* involving an isolated antibody with this specificity.

Detection methods involving isolated antibodies having the specificity recited in claim 16 and 31 are also not inherently disclosed by Norgard. "[A]nticipation by inherent disclosure is appropriate only when the reference discloses prior art that must *necessarily* include the unstated limitation" (Transclean Corp. v. Bridgewood Services, Inc., 290 F.3d 1364, 1373, 62 USPQ2d 1865, 1871 (Fed. Cir. 2002); emphasis in original). Moreover, "[i]n relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art" (*Ex parte* Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Int'f 1990); emphasis in original). "Inherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient" (*In re* Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999); emphasis added).

In the present case, isolated anti-*T. pallidum* antibodies "specific for an immunogenic peptide of *T. pallidum* acidic repeat protein . . . compris[ing] the amino acid sequence $EVEDX_1PX_2VVEPASX_3X_4EGGER$, wherein X_1 is A or V; X_2 is K or G; X_3 is E or G; and X_4 is R or H . . . ." do not *necessarily flow* from the Norgard disclosure. Norgard discloses only

thirteen monoclonal antibodies for use in detecting *T. pallidum* organisms (see, *e.g.*, Abstract and Table 1 in Norgard). Eight of Norgard's monoclonal antibodies are specific for the same 47 kD *T. pallidum* protein (see, Norgard at page 715, "Western blot analyses" and at page 716, column 1, first full sentence). The antibodies recited in claims 16 and 30 bind to an "immunogenic peptide of [a] *T. pallidum* acidic repeat protein." The molecular weight of a *T. pallidum* acidic repeat protein is 59.4 kD (see, specification at page 30, line 23). The 47 kD protein recognized by the foregoing eight Norgard antibodies is considerably smaller than a 59.4 kD *T. pallidum* acidic repeat protein. Moreover, the amino acid sequences of the *T. pallidum* 47 kD protein and acidic repeat protein are now known and there is no appreciable sequence homology between these proteins. Accordingly, it is not even possible (much less *necessarily* true) that those eight Norgard antibodies have the specificity of the antibodies recited in claim 16 or 31.

The Examiner must be taking the position that an isolated antibody "specific for an immunogenic peptide of *T. pallidum* acidic repeat protein . . . compris[ing] the amino acid sequence $EVEDX_1PX_2VVEPASX_3X_4EGGER$, wherein X_1 is A or V; X_2 is K or G; X_3 is E or G; and X_4 is R or H . . . ." *necessarily flows* from Norgard's disclosure of five monoclonal antibodies having specificities for some unknown *T. pallidum* antigen(s). However, as discussed below, this position is not supported by the facts.

A useful description of antibody technology is provided in the Background of Hybritech Inc. v. Monoclonal Antibodies, Inc. (802 F.2d 1367, 1368-1370, 231 USPQ 81, 82-83 (Fed. Cir. 1986)). As explained in that case (and as commonly known in the art), a monoclonal antibody is "directed to only one epitope on an antigen" (Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1369, 231 USPQ 81, 82 (Fed. Cir. 1986)). Thus, at best, Norgard's five uncharacterized antibodies can be specific for **only five epitopes on, at most, five different *T. pallidum* antigens**. For an isolated antibody having the specificity recited in claims 16 and 30 to *necessarily* flow from the disclosure of these five Norgard antibodies, the Examiner must assume that there are only five possible specificities for **all** possible isolated anti-*T. pallidum* antibodies. This assumption is clearly not true.

As summarized by the *Hybritech* court, "any foreign molecule [(or antigen)] of sufficient size can act as a stimulus for antibody production" (802 F.2d 1367, 1368, 231 USPQ 81, 82 (Fed.

Cir. 1986)). *T. pallidum* proteins, nucleic acids, polysaccharides and other biomolecules can serve as antigens for the production of anti-*T. pallidum* antibodies. There are thousands of such possible antigens. For example, it is known that *T. pallidum* expresses over 1000 proteins (see, for example, the list of proteins encoded by the complete *T. pallidum* genome, which is publicly available at ftp.ncbi.nih.gov/genomes/Bacteria/Treponema_pallidum/NC_000919.ptt). Even considering only *T. pallidum* protein antigens and assuming each protein antigen had only one antibody binding site (whereas multiple epitopes per antigen commonly occur), the number of possible anti-*T. pallidum* antibodies that could be isolated **vastly** exceed the five "uncharacterized" monoclonal antibodies described by Norgard.

The "examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art" (*Ex parte* Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Int'f 1990); emphasis in original). Thus, in this case, the Examiner must show that Norgard *necessarily* teaches methods employing an antibody specific for an immunogenic peptide of *T. pallidum* acidic repeat protein as recited in claims 16 and 31. In light of the many thousands (perhaps more) of possible isolated anti-*T. pallidum* antibodies that can be envisioned, it is **extremely unlikely** that one of the five "uncharacterized" Norgard antibodies is ". . . specific for an immunogenic peptide of *T. pallidum* acidic repeat protein . . . compris[ing] the amino acid sequence $EVEDX_1PX_2VVEPASX_3X_4EGGER$, wherein X_1 is A or V; X_2 is K or G; X_3 is E or G; and X_4 is R or H . . . ." As a result, the Examiner has not met her burden to show "the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art." Moreover, the Examiner has provided no basis in fact and/or technical reasoning that would support such a contention. Thus, the elements of claims 16 and 31 are not inherently disclosed in the cited reference, and the rejection should be overturned.

2. Hunter Does Not Inherently Anticipate Claims 1-2, 5-7, 11-16, and 30-31 under 35 U.S.C. §102(b)

A. *Hunter's "method of detecting syphilis . . . using desoxycholate-extracted treponemal antigen" Does Not Expressly or Inherently Disclose the Claim 16 or 31 Detection Method Using an Isolated Antibody*

To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently (see, *e.g.*, Glaxo Inc. v. Novopharm Ltd., 52 F.3d 1043, 1047, 34 USPQ2d 1565, 1567 (Fed. Cir. 1995)).

The Examiner states that "Hunter et al teach a method of detecting syphilis in sera samples using desoxycholate-extracted treponemal **antigen** (i.e., isolated) . . . ." (8/16/04 Advisory Action at page 4, and 3/2/04 Office Action at pages 5-6; emphasis added). As discussed in detail in Argument 1 (above), claims 16 and 31 recite a method involving isolated anti-*T. pallidum* **antibodies** having a particular protein specificity.

Hunter does not expressly or inherently teach **any** isolated antibodies at all, and certainly does not teach isolated antibodies with the specificity of those recited in claims 16 and 31. Because Hunter does not expressly or inherently teach all of the elements of claims 16 and 31, Hunter can not anticipate these claims. Therefore, Applicants request that this rejection of claims 16 and 31 be overturned.

B. The Examiner Admits that Hunter "May" Disclose an Allegedly Inherent Limitation of Claims 1, 2, 5-7, 11-15, and 30

To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently (see, *e.g.*, Glaxo Inc. v. Novopharm Ltd., 52 F.3d 1043, 1047, 34 USPQ2d 1565, 1567 (Fed. Cir. 1995)). At least one limitation of the method of claim 1 and its dependent claims 2, 5-7, 11-15, and 30 is not expressly or inherently disclosed by Hunter. In particular, claim 1 and its dependent claims 2, 5-7, 11-15, and 30 recite a detection method involving, in relevant part, an isolated "acidic repeat protein or . . . isolated immunogenic *Treponema pallidum* peptide(s) of the acidic repeat protein compris[ing] the amino acid sequence $EVEDX_1PX_2VVEPASX_3X_4EGGER$, wherein X_1 is A or V; X_2 is K or G; X_3 is E or G; and X_4 is R or H."

Hunter does not expressly disclose the foregoing claim limitation. The Examiner admits this fact by relying solely on the doctrine of inherent anticipation for her rejection.

The Examiner supports this inherent anticipation rejection "on the grounds that Hunter et al teach a method of detecting syphilis in sera samples using desoxycholate-extracted treponemal antigen (i.e., isolated) . . . . The sequence of the *T. pallidum* peptide, for example SEQ ID NO: 15 would be inherent in the teachings of the prior art" (8/16/04 Advisory Action at page 4, and 3/2/04 Office Action at pages 5-6). However, Hunter does not inherently disclose the specific acidic repeat protein or its immunogenic peptide as recited in claims 1, 2, 5-7, 11-15, and 30.

As discussed above, "[a]nticipation by inherent disclosure is appropriate only when the reference discloses prior art that must *necessarily* include the unstated limitation" (Transclean Corp. v. Bridgewood Services, Inc., 290 F.3d 1364, 1373, 62 USPQ2d 1865, 1871 (Fed. Cir. 2002); emphasis in original). Moreover, "[i]n relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art" (*Ex parte* Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Int'f 1990); emphasis in original). "Inherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient" (*In re* Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999); emphasis added).

The Examiner expressly admits that "[a]lthough the desoxycholate extract . . .contains 'an unknown mixture of some fraction of *T. pallidum* proteins', this <u>does not exclude</u> the fact that the claimed *T. pallidum* acidic repeat protein <u>may be included</u> in the unidentified *T. pallidum* protein mixture" (8/16/04 Advisory Action at page 5; emphasis in original). The fact that an unstated claim limitation "<u>may be included</u>" in a reference is **not** sufficient basis for an inherent anticipation rejection. The Examiner expressly offers only "probabilities or possibilities" in support of this inherent anticipation rejection. As explained by the *In re* Robertson court (169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999)), such probabilities or possibilities are an improper basis for an inherent anticipation rejection. Thus, Applicants request that this rejection be overturned.

With further regard to claim 5, Hunter does not disclose every limitation of claim 5, either explicitly or inherently (see, *e.g.*, Glaxo Inc. v. Novopharm Ltd., 52 F.3d 1043, 1047, 34 USPQ2d 1565, 1567 (Fed. Cir. 1995)). In particular, Hunter does not disclose an isolated "immunogenic peptide compris[ing] an amino acid sequence having the sequence shown in SEQ ID NO: 15." Thus, Hunter can not anticipate the method of claim 5.

Hunter discloses a sodium desoxycholate extract of *T. pallidum*. Hunter explains that the extract is prepared using the procedure of Portnoy and Magnuson, (*J. Immunol.*, 75(5):348-55, 1955) with only minor modifications (see page 483, column 2, "SD extraction" in Hunter). Neither Hunter nor Portnoy and Magnuson identify the proteins or other components contained in the sodium desoxycholate extract (by protein sequence or otherwise). In fact, Portnoy and Magnuson expressly state that "limited information available does not permit chemical characterization of the [desoxycholate extract]" (see page 352, column 2 in Portnoy and Magnuson). Accordingly, as recognized by the Examiner (see 8/16/04 Advisory Action at page 5), Hunter (and Portnoy and Magnuson) discloses an **unknown mixture of some fraction of *T. pallidum* proteins** (and possibly other cellular components).

By definition, the components of an "unknown mixture" are uncertain, indefinite, and not fixed, clear, or precise. Thus, it can not (and does not) *necessarily* flow that a specific immunogenic peptide having a particular amino acid sequence (as recited in claim 5) is contained within an unknown mixture of some fraction of *T. pallidum* proteins. In fact, because sodium desoxycholate solubilizes predominantly membrane proteins and the *T. pallidum* acid repeat protein lacks a lipid anchor, the acid repeat protein is *very unlikely* to be present in a desoxycholate extract and certainly is not *necessarily* present in such an extract. Thus, the Examiner has not met her burden to show "the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art." Applicants request that this rejection of claim 5 be overturned.

With further regard to claim 30, Hunter does not expressly or inherently disclose every limitation of claim 30 (see, *e.g.*, Glaxo Inc. v. Novopharm Ltd., 52 F.3d 1043, 1047, 34 USPQ2d 1565, 1567 (Fed. Cir. 1995)). In particular, Hunter does not disclose:

". . . [a] repeat region of the acidic repeat protein compris[ing] an amino acid sequence selected from any sequence comprising: $EVEDX_1PX_2VVEPASX_3X_4EGGEREVEDX_1PX_2VVEPASX_3X_4EGGER$ (wherein X_1 is A or V; X_2 is K or G; X_3 is E or G; and X_4 is R or H), which has an immunogenicity specific to *Treponema pallidum*."

The Examiner admits that Hunter discloses an **unknown mixture of some fraction of *T. pallidum* proteins** (and possibly other cellular components) (see 8/16/04 Advisory Action at page 5). As previously established, the components of an "unknown mixture" are uncertain, indefinite, and not fixed, clear, or precise. Thus, it can not (and does not) *necessarily* follow that a repeat region of an acidic repeat protein having a particular amino acid sequence (as recited in claim 30) is disclosed by an unknown mixture of some fraction of *T. pallidum* proteins. Thus, the Examiner has not met her burden to show "the allegedly inherent characteristic [of claim 30] *necessarily* flows from the teachings of the applied prior art." Applicants request that this rejection of claim 30 be overturned.

3. Hunter Does Not Render Obvious Claim 28 under 35 U.S.C. §103(a)

In order to establish a *prima facie* case of obviousness, the Examiner must offer (among other things) references that teach or suggest all of the elements of the rejected claim (*In re* Royka, 490 F.2d 981, 984, 180 USPQ 580, 582 (CCPA 1974)). Claim 28 recites, in relevant part, ". . . the method of claim 1." As discussed above in Argument 2, Hunter does not teach or suggest all of the elements of claim 1. In particular, Hunter does not teach or suggest an isolated "acidic repeat protein or . . . isolated immunogenic *Treponema pallidum* peptide(s) of the acidic repeat protein compris[ing] the amino acid sequence $EVEDX_1PX_2VVEPASX_3X_4EGGER$, wherein X_1 is A or V; X_2 is K or G; X_3 is E or G; and X_4 is R or H." Thus, all the claim limitations of claim 28 are not taught or suggested by Hunter, and the Examiner has not cited any other reference(s) that makes up for the failings of the cited reference. Accordingly, a *prima facie* case of obviousness is not established (see, *e.g.*, MPEP §1504.03). The Examiner has failed to overcome the burden of establishing a *prima face* case of obviousness; therefore, this rejection of claim 28 should be overturned.

For one or more of the foregoing reasons, it is submitted that the Examiner's rejections are erroneous. Accordingly, reversal of the Examiner's decision and allowance of the rejected claims are respectfully requested.

Respectfully submitted,

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Attorney Reference Number 6395-61666-01
Application Number 10/017,168
EXPRESS MAIL LABEL NO. EV331579945US
DATE OF DEPOSIT: OCTOBER 12, 2004

CLAIMS APPENDIX

1. A method of detecting the presence of *Treponema pallidum* or anti-treponemal antibodies in a biological sample, comprising:

contacting an isolated *Treponema pallidum* acidic repeat protein or one or more isolated, immunogenic *Treponema pallidum* peptide(s) of the acidic repeat protein with an antibody-containing biological sample, wherein the acidic repeat protein or the isolated immunogenic *Treponema pallidum* peptide(s) of the acidic repeat protein comprises the amino acid sequence $EVEDX_1PX_2VVEPASX_3X_4EGGER$, wherein X_1 is A or V; X_2 is K or G; X_3 is E or G; and X_4 is R or H; and

detecting formation of a complex between the immunogenic protein or peptide and the antibody, wherein the presence of the complex indicates the presence of *Treponema pallidum* or anti-treponemal antibodies in the biological sample.

2. The method of claim 1, wherein the isolated, immunogenic *Treponema pallidum* peptide comprises a repeat region of the acidic repeat protein.

5. The method of claim 1, wherein the immunogenic peptide comprises an amino acid sequence having the sequence shown in SEQ ID NO: 15.

6. The method of claim 1, wherein the *Treponema pallidum* is *T. pallidum* subspecies *pallidum*, *T. pallidum* subspecies *pertenue* (CDC-2 strain), *T. pallidum* subspecies *pertenue* (CDC-1 strain), or *T. pallidum* subspecies *endemicum*.

7. The method of claim 1, wherein detecting the presence of the complex indicates the presence of the disease syphilis, yaws, or bejel.

11. The method of claim 1, wherein the acidic repeat protein or immunogenic peptide is bound to a solid phase.

12. The method of claim 1, wherein the acidic repeat protein or immunogenic peptide is labeled.

13. The method of claim 12, wherein the label comprises an electrochemiluminescent label, a chemiluminescent label, an enzymatic label, a bioluminescent label, or a fluorescent label.

14. The method of claim 1, further comprising incubating the peptide-antibody complex with a second antibody specific for the peptide, wherein the second antibody is labeled with a detectable label and binds to the peptide-antibody complex.

15. The method of claim 1, wherein the biological sample comprises wounds, blood, tissues, saliva, semen, vaginal secretions, tears, urine, bone, muscle, cartilage, CSF, skin, or any human tissue or bodily fluid.

16. A method of detecting the presence of *Treponema pallidum* in a biological sample, comprising:

contacting an isolated antibody specific for an immunogenic peptide of *T. pallidum* acidic repeat protein with a biological sample, wherein the acidic repeat protein comprises the amino acid sequence $EVEDX_1PX_2VVEPASX_3X_4EGGER$, wherein X_1 is A or V; X_2 is K or G; X_3 is E or G; and X_4 is R or H; and

detecting formation of a complex between the acidic repeat protein or a peptide of the acidic repeat protein, if such is in the biological sample, and the antibody, wherein the presence of the complex indicates the presence of *Treponema pallidum*.

28. A kit for detecting *T. pallidum* in a biological sample using the method of claim 1, comprising an isolated acidic repeat protein or one or more isolated, immunogenic *Treponema pallidum* peptide of the acidic repeat protein, and instructions for carrying out the method of claim 1.

30. The method of claim 2, wherein the repeat region of the acidic repeat protein comprises an amino acid sequence selected from any sequence comprising:

$EVEDX_1PX_2VVEPASX_3X_4EGGEREVEDX_1PX_2VVEPASX_3X_4EGGER$

(wherein X_1 is A or V; X_2 is K or G; X_3 is E or G; and X_4 is R or H), which has an immunogenicity specific to *Treponema pallidum*.

31. The method of claim 16, wherein the immunogenic peptide comprises a repeat region of the acidic repeat protein.

EVIDENCE APPENDIX

[None]

RELATED PROCEEDINGS APPENDIX

[Not applicable]